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Electrophysiology in Ménière's Disease

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<http://dx.doi.org/10.5772/intechopen.69668>

Abstract

Ménière's disease (MD) is a progressive inner ear disorder that affects at least 0.2% of the population in EUA. The symptoms triad of fluctuating hearing loss, tinnitus, and vertigo was described by Prosper Ménière for more than a century and its pathophysiology is still unknown. MD has a fluctuating course and in many cases, difficult clinical management. Progressive hearing loss and intense dizzying seizures becomes more frequent as the disease progresses. All of this increases the challenges of accurate identification and has probably led to the trial of several tests for identifying MD. The tests are useful tools to assist the otolaryngologist both in diagnosis and prognosis of MD. These tests includes audiometry, otoacoustic emission (OAE), electrocochleography (EcochG), vestibular evoked myogenic potentials (VEMP), cochlear hydrops analysis masking procedure (CHAMP) and video head impulse test (vHIT).

Keywords: Meniere's disease, endolymphatic hydrops, electrocochleography, VEMP, CHAMP, vHIT

1. Introduction

Ménière's disease (MD) is a progressive inner ear disorder that affects at least 0.2% of the population in EUA [1]. The symptoms triad of fluctuating hearing loss, tinnitus, and vertigo was described by Prosper Ménière for more than a century and its pathophysiology is still unknown.

For a long time, it was believed that endolymphatic hydrops would be the histopathological substrate of the disease. The cause of hydrops is still unknown and most of the theories are based on altered endolymph production or reabsorption. The hydrops occurs more often in the cochlea and saccule, followed by the utricle and semicircular channels [2]. Recent studies have indicated that hydrops is a finding of the MD, together with the symptoms, since it

alone does not explain all the clinical features, including the progression of hearing loss and the frequency of vertigo attacks [3].

According to the criteria of the Bárány Society, MD is classified as definite or probable. In definite MD, the patient should have had two or more spontaneous episodes of vertigo, each lasting from 20 min to 12 h, documented mild to moderate sensorineural hearing loss, aural symptoms (hearing, tinnitus, and fullness) in the affected ear, and exclusion of other vestibular disorders that explain the symptoms. In probable MD, the patient should have had two or more episodes of vertigo or loss of balance, each lasting from 20 min to 24 h, floating aural symptoms (hearing, tinnitus, or fullness) in that ear, and exclusion of other vestibular disorders that explain the symptoms [4].

MD has a fluctuating course and in many cases difficult in clinical management. Progressive hearing loss becomes more frequent and intense dizzying seizures as the disease progresses. All of this increases the challenges of accurate identification, and has probably led to the trial of several tests for identifying MD. The tests are useful tools to assist the otolaryngologist both in diagnosis and prognosis of MD. Identify the site of hydrops, even in cases of severe hearing loss and possible involvement of the asymptomatic ear are useful information on disease management.

These tests includes tonal and speech audiometry /impedance, otoacoustic emissions (OAE), electrocochleography (EcochG), vestibular evoked myogenic potentials (VEMP), cochlear hydrops analysis masking procedure (CHAMP) and video head impulse test (vHIT).

2. Electrophysiology

2.1. Tonal and speech audiometry/Impedance

Audiometry is helpful to confirm the diagnosis and it is a part of the criteria of the Bárány Society. In the early stages of the disease, there is a low frequency sensorineural hearing loss that fluctuates in time. In some cases, it also affects high frequency, setting the pattern of inverted U. In later stages, the hearing loss would increase and the audiogram would become more and more flat. Sometimes, a decreased speech discrimination is also mentioned as a common symptom of MD [5]. Hearing loss initially resolves after attacks, but with the disease progression, patients may experience loss of auditory nerve fibers. The impedance is helpful to exclude middle ear pathology.

2.2. Otoacoustic emission (OAE)

Otoacoustic emissions are subliminal sounds detected in the external auditory canal and generated by the outer hair cells. They are useful in the diagnosis of many cochleopathies, including MD.

Authors believe that hydrops causes changes in the hydrodynamic and cochlear biomechanical micromechanism, due to changes in the interciliary bridges caused by the distension of

membranes and cells within the cochlear duct. These changes could affect the transmission of the stimulus by outer hair cells, but not necessarily loss of them. The selective atrophy of the short and medium stereocilia at the cochlea's apex is correlated with the hearing loss in low frequencies that occur in the early phase of MD. The OEA can reveal early lesions due to alterations of the cochlear micromechanism not correlated with the auditory thresholds detected in tone audiometry [6].

The distortion product otoacoustic emission (DPOAE) was considered more appropriate than transient otoacoustic emission (TEOAE) for monitoring during glycerol test because of its high sensitivity in the detection of changes in cochlear function. DPOAE is a complementary test to pure tone audiometry during the glycerol test. It is very useful and will improve the diagnosis of endolymphatic hydrops [7].

2.3. Electrocochleography (EcochG)

Electrocochleography records the three mechano-electrical potentials of the cochlea. The cochlear microphonic is considered the first step to the neural impulse. It reflects the sum of the intracellular potentials generated in the hair cells of the basal portion of the cochlea during depolarization [8]. Hall in 2007, Durrant, Ding and Salvi in 1998, affirm that the inner hair cells play a central role in the generation of SP, while other authors, such as Burkand et al. believe that it is generated by both internal and external hair cell [8–10]. Action potential (AP) is the sum of the synchrony of individual neural APs of the cochlear nerve.

Electrocochleography is the test capable of measuring endolymphatic hydrops in the cochlea. The test is usually performed with a transtympanic or extratympanic electrode (**Figure 1**). Hydrops changes the mechanical properties of the cochlea, leading to asymmetric movements of the basilar membrane, which may exacerbate the SP, and consequently, increases the ratio between the amplitudes of SP and AP. The increase in SP amplitude will change according to the existing pressure and volume of the intralabyrinthine fluid [10, 11] (**Figure 2**).

The SP/AP ratio thresholds are variable in the literature. Pappas et al. believe that any result above 0.5 in an extratympanic EcochG is suggestive of endolymphatic hydrops [12], while Iseli and Gibson established a value of 0.33 in a transtympanic EcochG [13].

Lamounier et al. in a systematic review reported that in 25–54% of patients with MD, the electrocochleography presented normal results, with the sensitivity of the test ranging from 57 to 71% and a specificity ranging from 92 to 96%. In most studies selected, the transtympanic electrode is the most widely used. EcochG in MD presents a variable sensitivity, as in cases of hearing loss due to disease progression, patients may experience a reduction in the amplitude of AP due to loss of auditory nerve fibers [14–17].

On comparing the results of the transtympanic and extratympanic electrocochleography in 20 patients with Ménière's disease and 20 control patients, Ghosh et al. reported a significant difference between the SP/AP ratios of the cases and control groups. For an SP/AP ratio of 0.29, they found 100% sensitivity, 90% specificity to transtympanic, and 90% and 80% to the extratympanic EcochG, respectively, and concluded that extratympanic EcochG is a non-invasive method, effective and easier to carry out in clinical practice than transtympanic EcochG [15].

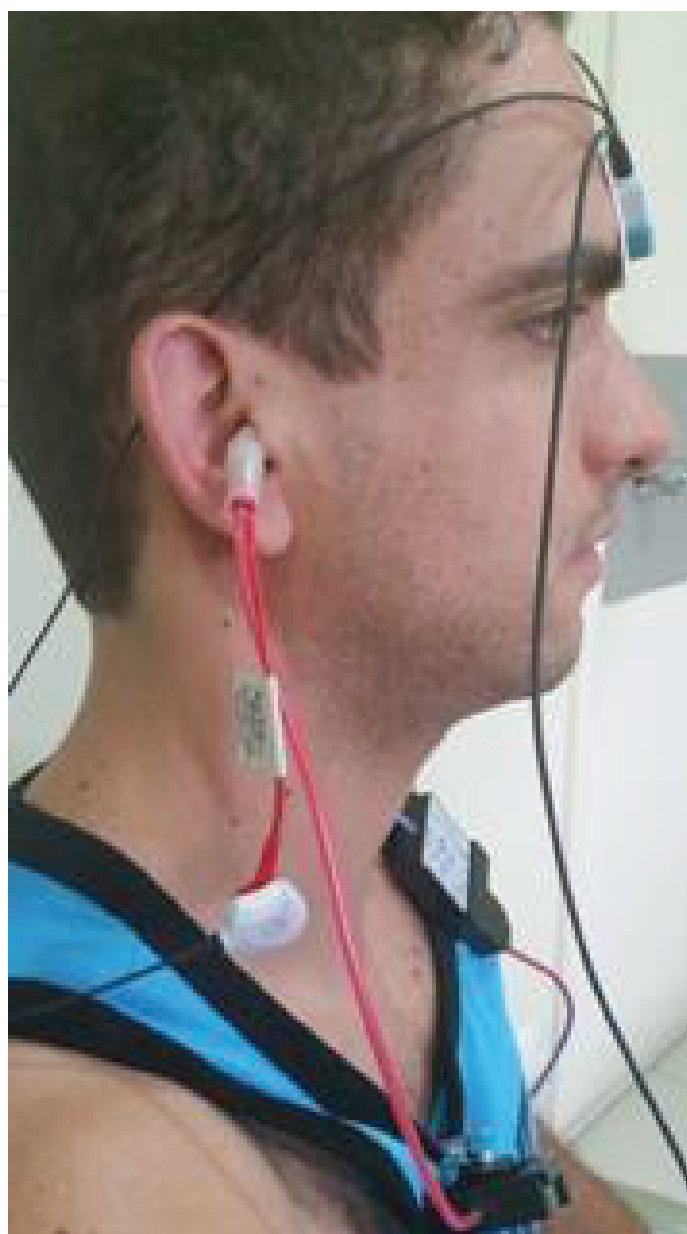


Figure 1. Position of EcochG's electrodes.

Lamounier et al. also found in the systematic review that the analysis of the SP/AP ratio curve of the transtympanic electrocochleography did not necessarily increase sensitivity in the diagnosis of hydrops when compared with the SP/AP amplitude [14, 16–18].

Gibson et al. compared EcochG results in ears with Ménière's disease and healthy ears with similar hearing loss and concluded that click SP/AP measurements are not helpful in making this differentiation but that tone burst SP amplitude measurements were significantly different between these populations [19].

Colon and Gibson showed that the sensitivity of transtympanic electrocochleography increased to 85% when 1 kHz of tone burst was used to measure SP. They reported that the majority of

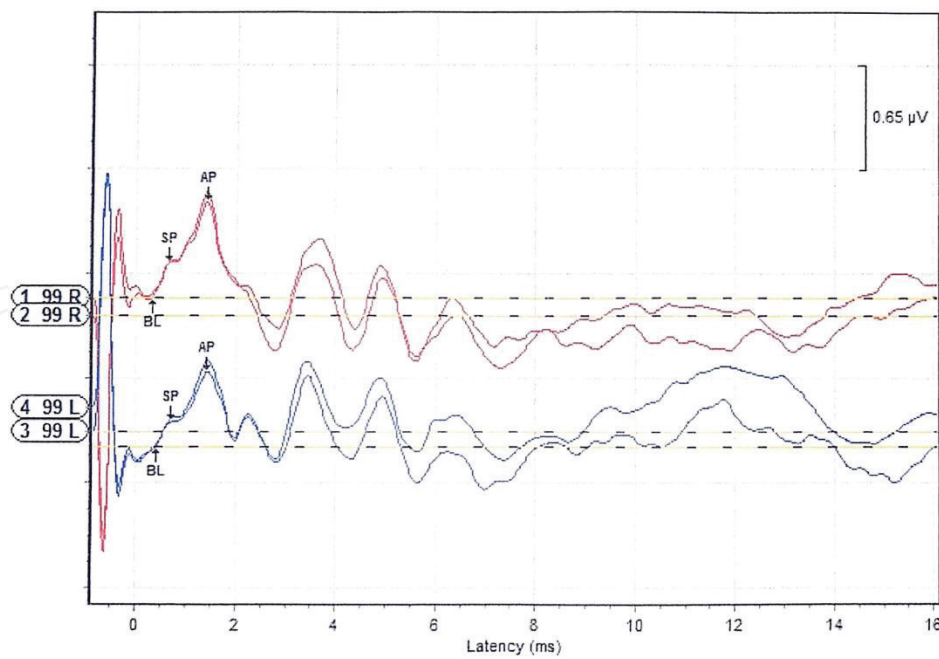


Figure 2. EcochG.

specialists or 58.6%, use click stimuli as opposed to 17.2%, who use tone burst, and 24.3% who use both stimuli [20]. Lopes et al. evaluated the sensitivity and specificity of the SP/AP ratio and graphic angular measurement in electrocochleographies of 71 ears of 41 MD patients and 14 normal-hearing control patients. They concluded that the graphic angular measurement is not sensitive or specific enough to diagnose MD. The association of the SP/AP ratio and graphic angular measurement in conjunction improved the sensitivity to the detriment of the specificity of the test [21].

Electrocochleography is a valuable tool in the diagnosis of cochlear hydrops, as it is noninvasive, easy to handle, and offers new techniques to increase the sensitivity of the test.

2.4. Vestibular evoked myogenic potentials (VEMP)

Vestibular evoked myogenic potentials (VEMP) emerged as a recent and complementary way of vestibular system assessment with the specific analysis of the saccular function and inferior vestibular nerve.

In 1992, Colebatch and Halmagyi proposed that the saccular macula was the peripheral receptor of the vestibular-spinal reflex and in 1994 reported surface potential in the sternocleidomastoid (SCM) muscle in response to clicks through high-intensity air conduction (100 dB), accessing the Sacculo-collic reflex [22].

VEMP is, therefore, a short latency myogenic response, generated after a sound stimulus, originating in the sacculo and conducted by the inferior division of the inferior vestibular nerve to the central nervous system, generating inhibitory electrical responses captured by surface electrodes on the muscles, during muscular contraction. This neural response is a reflex arc of three neurons that surround the inner ear, the brainstem, and the vestibular-spinal pathway [22–24] (**Figure 3**).

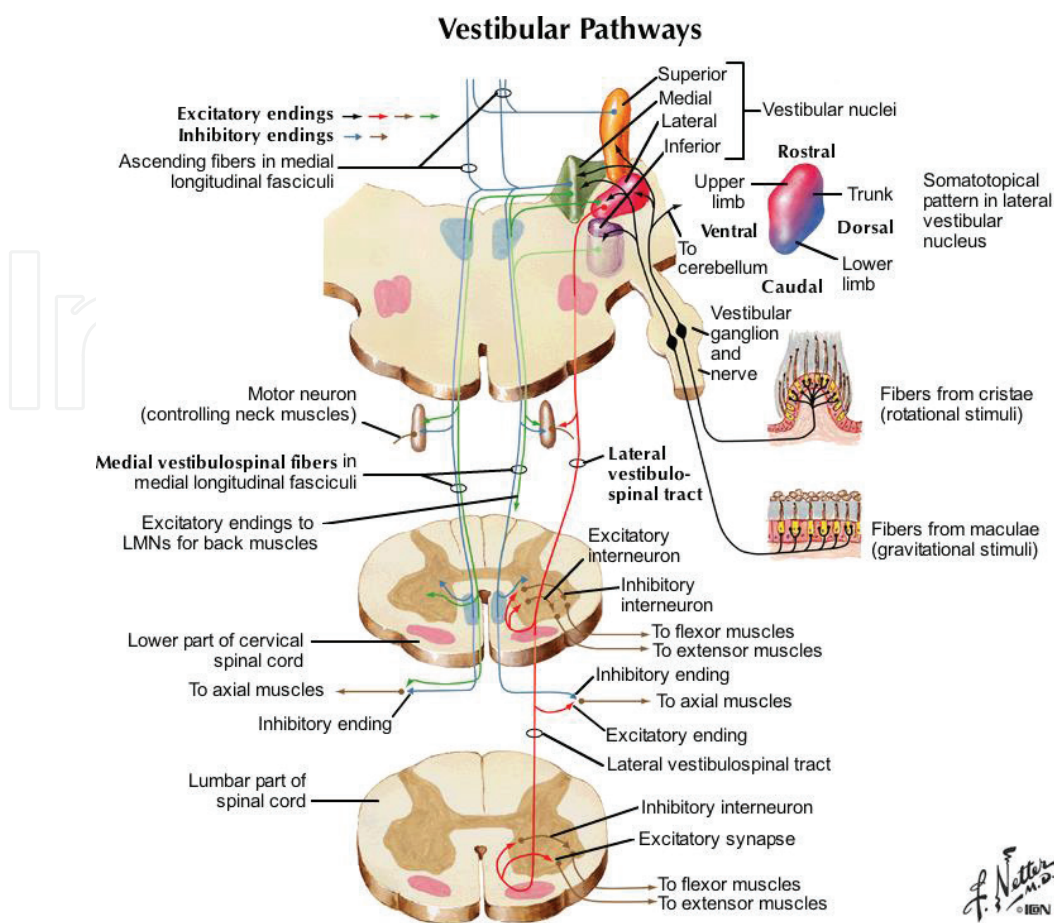


Figure 3. Neural pathway of VEMP.

Similar myogenic responses have been captured in other muscle groups. The responses captured in SCM are called cervical VEMP (cVEMP) and those collected in the extraocular musculature are called ocular VEMP (oVEMP). VEMP can be obtained by air and bone conduction and galvanic stimulation, using tone burst or clicks stimulus [23–25] (**Figure 4**).

The electrical responses of these potentials consist of two biphasic waves, the first negative wave, with latency around 13 ms, known as p13. This is followed by another wave, this time positive, with latency around 23 ms, known as n23. There is also a second biphasic complex known as n34-p44, but due to the lack of replicability of this second complex, only the first complex is considered. The electromyographic potential recording waves are usually defined by: latency, wave morphology, peak-to-peak amplitude, or the difference in values between the most positive point of one wave and the most negative point of another wave [26] (**Figure 5**).

The large variation in the amplitude of the responses, due to the different degrees of muscular contracture obtained for each individual, justifies the analysis of the VEMP responses through the interaural asymmetry index. The literature review showed that VEMP is considered altered by the absence of reproducible waves and or asymmetry index of interaural responses greater than 34% [26].

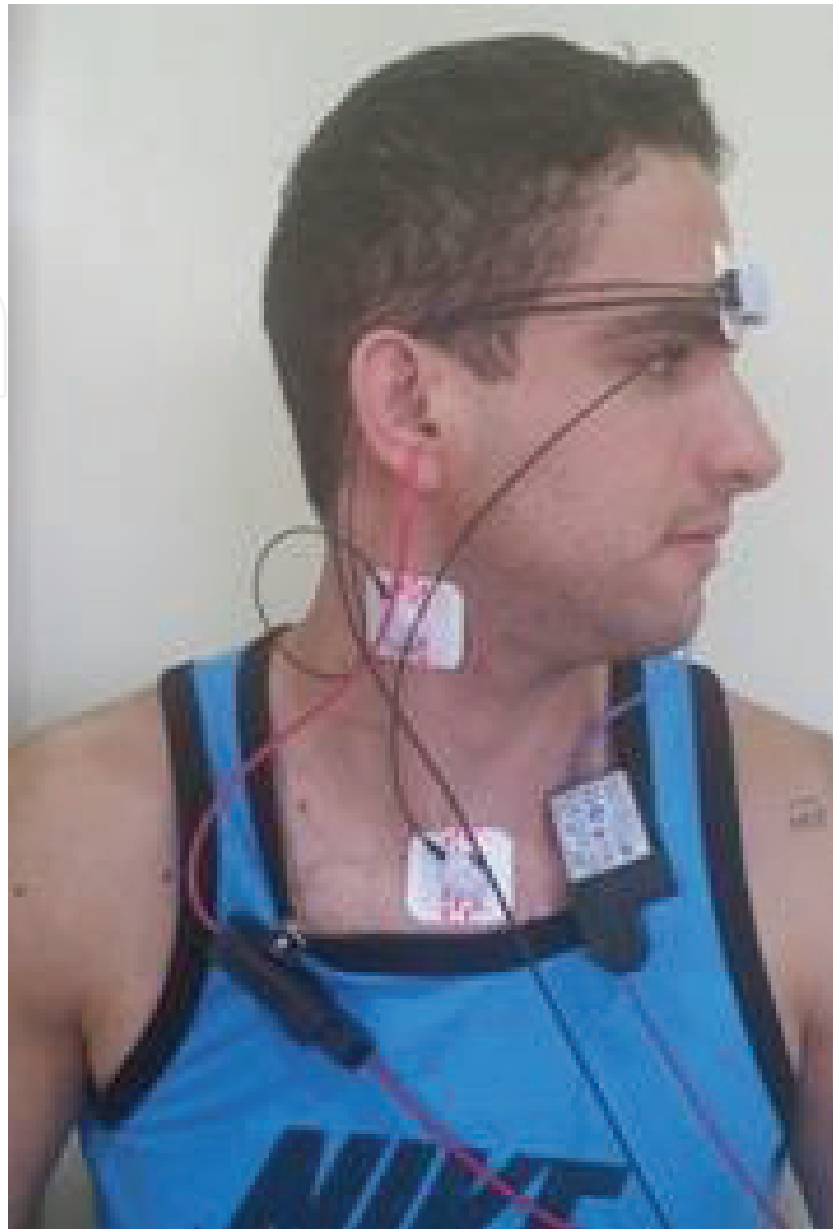


Figure 4. Position of cervical VEMP's electrodes.

The cVEMP is more sensitive for deep bass. Stimuli with frequencies near 500 Hz have higher response amplitudes. Air conducted (AC) sound is the most commonly used stimulus for eliciting cVEMPs. Tone bursts are preferable above clicks because the latter have less reliable results and need higher absolute intensities to evoke a response [26].

The cVEMP is absent or decreased by 30–54% in patients with MD [22, 23]. It may be increased in the early stages of MD, perhaps by the pressure of saccular hydrops against the stapes footplate, increasing sensitivity saccular to intense sound. Its measurement may be floating, with a tendency to disappear with the progression of the disease, as well as 24 h post-crisis, which may reappear after 48 h or with the use of drugs to reduce endolymphatic hydrops [25–27].

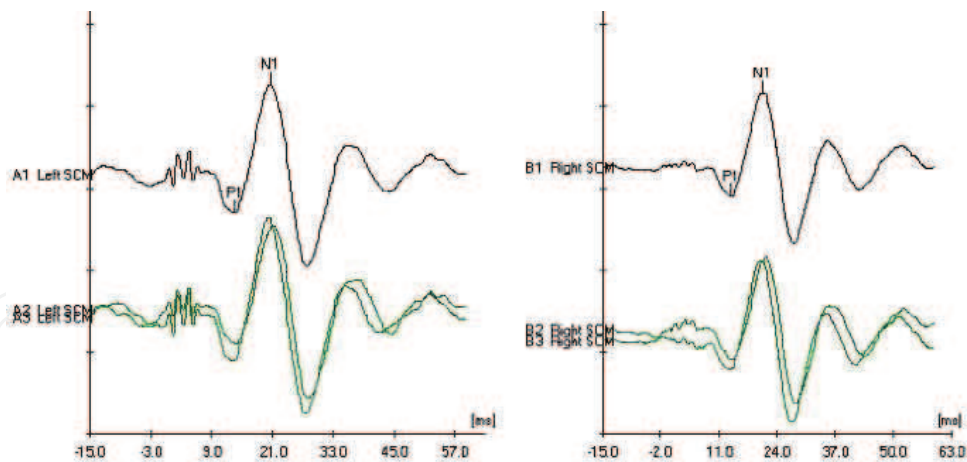


Figure 5. VEMP 's' waves.

Lamounier et al. evaluated the sensitivity and specificity of VEMP and EcochG in the diagnosis of definite MD compared with the clinical diagnosis. The study includes 12 patients (24 ears) diagnosed with definite MD defined according to the clinical criteria proposed by the American Academy of Otolaryngology Head and Neck Surgery (AAO-HNS) in 1995, as well as 12 healthy volunteers allocated to the control group (24 ears). A clinical diagnosis by the AAO-HNS criteria was considered as the gold standard. All patients underwent an otoneurological examination, including pure tone and speech audiometry, cVEMP and extratympanic EcochG. The sensitivity and specificity to detect the presence or absence of disease were calculated. In both tests and in both ears, the ability to diagnose healthy cases was high, with specificity ranging from 84.6 to 100%. Moreover, the ability of the tests to diagnose the disease varied from low to moderate sensitivity, with values ranging from 37.5 to 63.6%. The agreement of both tests in the right ear, measured by the kappa coefficient, was equal to 0.54 indicating a moderate agreement. In the left ear, that agreement was equal to 0.07 indicating a weak correlation between the tests. The sensitivity of the VEMP for the right ear was 63.6% and for the left ear, 62.5%. The sensitivity of EcochG for the right ear was 63.6% and 37.5% for the left ear. They concluded that the specificity of both tests was high, and the sensitivity of VEMP was higher than that of EcochG [3].

Similar to cVEMPs, oVEMPs can also be augmented in MD [28].

The ocular VEMP (oVEMP) is a more recently described reflex, which is thought to reflect predominantly utricular otolith function and can be understood as part of the vestibulo-ocular reflex (VOR). Patients with MD have higher rates of attenuated or absent oVEMPs than normal subjects, increasing with advancing disease [28–30].

Wen et al. recruited unilateral MD patients with either augmented or reduced oVEMPs (asymmetry >40 and <100%) in response to bone-conducted vibration and found that augmented oVEMPs were seen more frequently in patients with early stage MD. Augmented responses might also be more likely when recorded during an attack [31].

Winters et al. examined air-conducted oVEMPs in MD patients and found lower response rates with smaller amplitudes and higher thresholds compared to normal subjects. Interestingly,

this effect was observed not only in the affected, but to a lesser extent also in the clinically unaffected ears [32].

The VEMP is easy to perform, does not cause discomfort to patient and does not vary with hearing loss. The ability to predict the presence of abnormalities in an asymptomatic ear is one of the great features of VEMP [33].

2.5. Cochlear hydrops analysis masking procedure (CHAMP)

The cochlear hydrops analysis masking procedure (CHAMP) was introduced in 2005 as a new test to diagnose MD. Don et al. showed that endolymphatic hydrops in patients diagnosed with MD causes changes in the response properties of the basilar membrane that lead to impaired high-pass noise masking of auditory brainstem response (ABR) to clicks in stapedial ABR. The latency delay in normal-hearing ears, between wave V for the click alone response and the 0.5 kHz high-pass masking noise condition, is significantly longer than that in MD ears. This difference is known as the latency delay [34].

The increased velocity of the traveling wave would affect the properties of the basilar membrane but cannot affect the tonotopic organization along the basilar membrane. The increased velocity of the traveling wave is more likely to impact the low frequencies as they are represented toward the apical end on the basilar membrane. When ABR latencies are obtained by presenting clicks along with the high-pass masking noise in individuals with Ménière's disease, the altered motion mechanics of the basilar membrane limits the ability of low-frequency noise to mask the activity in high frequency [35, 36] (Figure 6).

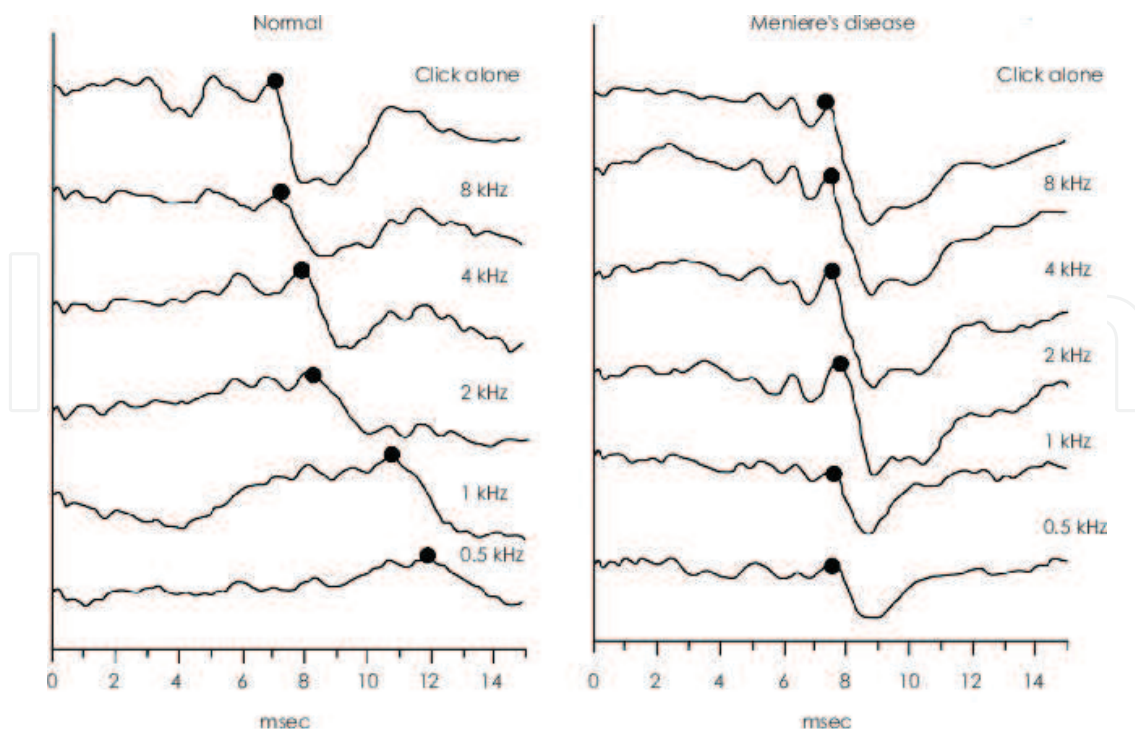


Figure 6. CHAMP.

In individuals with MD, we can observe the phenomenon of undermasking in high-pass responses, whereas the undermasking phenomenon is not seen in normal individuals. This would in turn result in lesser latency difference between click alone and click with 500 Hz high-pass masking noise condition in ears with MD than unaffected or normal ears [37].

Don et al. conducted the test in 23 definite MD patients and compared the results with 38 non-MD normal-hearing subjects. Their measures did not demonstrate an overlap between the Ménière's and nonMénière's groups, and therefore, the authors concluded that the test had an extremely high, even 100%, sensitivity and 100% specificity for diagnostic use in individual patients [34].

However, some studies have questioned these findings by reporting significantly lower sensitivity and specificity values. De Valck et al. evaluated CHAMP performance in Ménière patients and normal controls, and revealed no discriminative value in differentiating Ménière's from non-MD subjects with otovestibular symptoms [37].

Kingma investigated the usefulness of the cochlear hydrops analysis masking procedure (CHAMP) as an additional diagnostic test in patients with definite unilateral Ménière's disease. With less than 0.3 ms criterion and including the ears in which no delay could be measured, the sensitivity of the CHAMP is 32% and concluded that abnormal latency delays for CHAMP are delays shorter than 2 ms. Earlier results with CHAMP should be reconsidered using this criterion, instead of 0.3 ms [38].

Lee et al. suggest that the CHAMP seems to be more valuable in detection of definite MD than is extratympanic EcochG [39].

Furthermore, CHAMP can only be recorded for losses not exceeding moderate degree, which limits its use to identify Meniere's disease with lesser degree of hearing losses only.

The literature indicates a need for continued exploration of these tests in order to establish the usefulness or lack of it in the diagnosis for MD.

2.6. Video head impulse test (vHIT)

A new quantitative test of vestibular function known as the video head impulse test (vHIT) has recently emerged that now allows for discrete measurements of the vestibulo-ocular reflex (VOR) during evaluation of the extremely high-frequency head movements. Although the bithermal caloric test is useful for assessing low-frequency vestibular system function, the head impulse test (HIT), as described by Halmagyi and Curthoys, is a method for testing the function in a frequency region encountered in everyday life in the vestibular system [40, 41].

The primary differences between the vHIT and caloric tests are the mode of stimulus delivery (thermal gradient vs. natural head motion) as well as the temporal frequency of each examination (caloric stimulus represents a low-frequency stimulus and the vHIT a high-frequency stimulus). It is well known that the vHIT and caloric tests are sensitive to detection of a certain percentage of patients with MD [42, 43].

The test involves examiner-initiated high velocity, high-acceleration, and yet, small-amplitude head movements while the patient is instructed to stare at a stationary target

located at center gaze. If the VOR is intact, the patient will be able to maintain foveal vision of the target during the head impulse. If the VOR is impaired, rotation of the head toward the ipsilesional semicircular canal will drive the eyes off the target, forcing the patient to generate a volitional catch-up saccade to bring eyes back to the target [40] (Figures 7 and 8).

The receptor of the angular VOR is the crista ampullaris. This structure consists of both type I and type II hair cells as well as regularly and irregularly discharging afferent neurons. Type I hair cells populate the central part of the crista ampullaris. Irregular afferents primarily connect to type I hair cells or a mixture of type I and type II. These hair cells encode high-frequency, high-acceleration head movements. Type II cells populate the periphery of the crista. Regular afferents carry the output of type II hair cells or a mixture of type I and type II and likely encode low-frequency, low acceleration movement [44, 45].

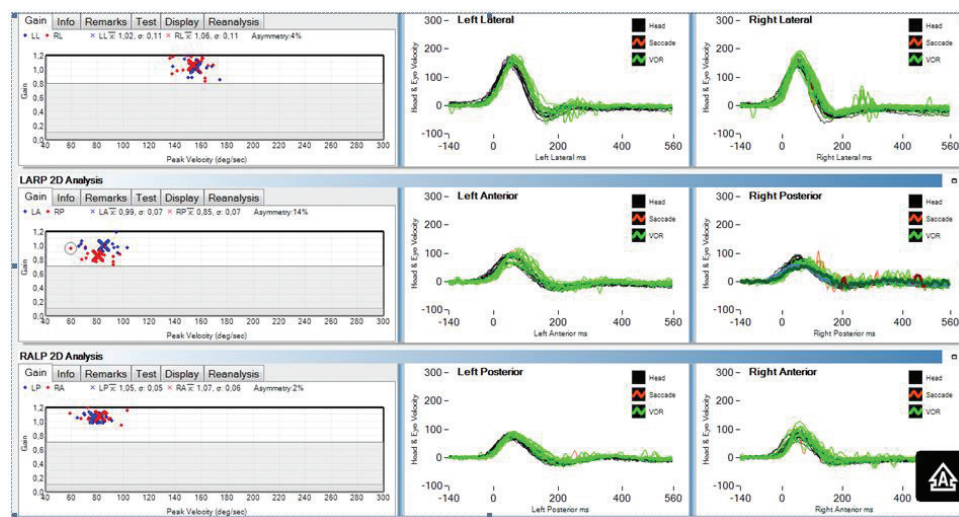


Figure 7. VHIIT : Speed of the head in black = speed the eyes in green. There is no record of corrective saccades. (Figure provided by borgesdecarvalhooortorinos.com.br).

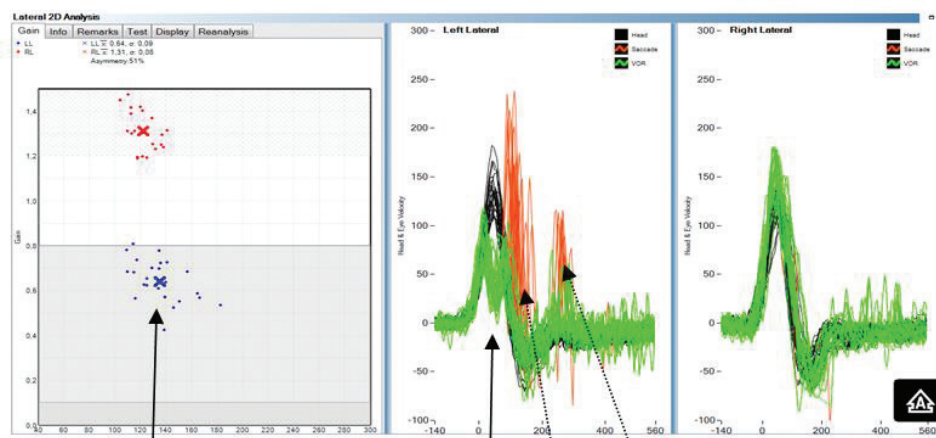


Figure 8. VHIIT: Lower eye velocity than head. Presence of saccades. (Figure provided by borgesdecarvalhooortorinos.com.br).

Tsuji et al. reported that although MD affected the structure and function of type II hair cells, the density and number of type I hair cells appeared unchanged in patients with MD [46].

Maire and van Melle showed that, in early stages of MD, VOR gain was higher when the patient was rotated toward the affected ear, but this observed enhancement diminished as the disease progressed [47].

McCaslin et al. presented three cases of patients with Ménière's disease with asymptomatic vestibular dysfunction demonstrated with videonystagmography (VNG) testing, which provided a quantitative measure of VOR gain. The authors found a dissociation between the caloric test and vHIT results, and they explained these findings by understanding the different dynamic response properties of the two primary populations of neurons in the crista [40].

The assessment of cochlear function with audiometry, EcochG and CHAMP, of the sacculus through cervical VEMP, of the utricle through ocular VEMP, of the lateral semicircular canal with the caloric tests, and all of the semicircular canals by the vHIT demonstrates the advancements of research in the vestibular diagnosis. New paths are open to the discovery of the pathophysiological mechanism of a disease that was first described over a century ago and still has no defined treatment protocol.

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